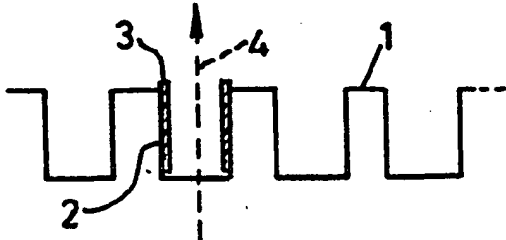
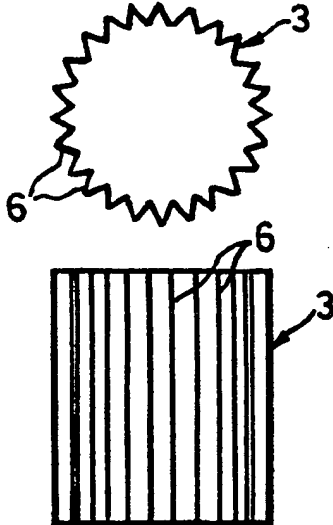




## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification <sup>5</sup> : <b>B01L 3/00, G01N 33/543</b></p>	<p><b>A1</b></p>	<p>(11) International Publication Number: <b>WO 91/06368</b></p> <p>(43) International Publication Date: <b>16 May 1991 (16.05.91)</b></p>
<p>(21) International Application Number: <b>PCT/GB90/01646</b></p> <p>(22) International Filing Date: <b>26 October 1990 (26.10.90)</b></p> <p>(30) Priority data: <b>8924252.3</b>                      <b>27 October 1989 (27.10.89)</b>      <b>GB</b></p> <p>(71)(72) Applicants and Inventors: <b>EDWARDS, Raymond [GB/GB]; 8 The Elms, Vine Road, Barnes, London SW13 0NS (GB). LITTLE, John, Alexander [GB/GB]; 57 Ormesby Way, Kenton, Middlesex HA3 9SE (GB).</b></p> <p>(74) Agent: <b>GODDARD, George, William, John; Hughes Clark &amp; Co., 63 Lincoln's Inn Fields, London WC2A 3JU (GB).</b></p>		<p>(81) Designated States: <b>AT (European patent), BE (European patent), CH (European patent), DE (European patent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent), US.</b></p> <p><b>Published</b> <i>With international search report.</i></p>
<p>(54) Title: <b>MICROTITRE PLATE WELL INSERTS</b></p> <div style="display: flex; justify-content: space-around; align-items: center;">   </div> <p>(57) Abstract</p> <p>The microtitre plate well inserts (2) of the present invention comprises a hollow tubular member with open ends the internal and/or external surface of which is shaped as a zig-zag or pleated wall (6) to provide an extended surface area for a reagent coated on the insert wall surface. Various other embodiments of the well insert are described including an insert formed as a helix and another in the form of a tube of open rectangular mesh.</p>		

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### MICROTITRE PLATE WELL INSERTS

This invention relates to well inserts for microtitre plates.

Microtitre plates having a plurality of circular wells are extensively used in diagnostic assays. A diagnostic reagent is coated, usually by passive absorption, onto the surface of a microtitre plate and measurement is made using some form of optical signal, such as fluorescence, luminescence or optical density.

10 The known microtitre plate requires mechanical strength for rigidity, absence of optical interference and a suitable surface for coating of the reagent, however these requirements are often incompatible with each other.

15 An aim of the present invention is to utilize the rigidity and optical qualities of known microtitre plates while improving the surface properties for the coating reagent.

According to the present invention there is provided a well insert for a microtitre plate comprising a hollow tubular member, the internal and/or external surface of which shaped to provide an extended surface area for a reagent coated on the surface, and the surface chemistry of which allows coating or covalent coupling of reagents.

Preferably, the insert is made of a plastics material such as polystyrene or polypropylene.

Embodiments of the present invention will now be described by way of example only with reference to the accompanying drawings, in which:

Figure 1 is a plan view of a microtitre plate fitted with well inserts according to the invention;

Figur 2 is a cross-section taken along th line 2-2 of Figure 1;

35 Figur 3 is a plan view and vertical cross-section of a first embodiment of a well insert;

Figure 4 is a plan view and a vertical cross-section of a second embodiment of a well insert;

Figure 5 is a plan view and a vertical cross-section of a third embodiment of a well insert;

Figure 6 is a plan view and a side elevation of a fourth embodiment of a well insert;

5 Figure 7 is a plan view and a side elevation of a fifth embodiment of a well insert;

Figure 8 is a side elevation of a sixth embodiment of a well insert, and

10 Figure 9 is a side elevation of a seventh embodiment of a well insert.

Figure 1 illustrates a plan view of a microtitre plate 1 made of a plastics material which has mechanical strength and enables the passage of light beams with the absence of optical interference. One such plastics material is polystyrene. However, when a reagent is placed in one of a plurality of wells 2 formed in the plate the reagent is unevenly coated on the internal surface of the well producing edge effects when e.g. an antibody diagnostic test is made.

20 To avoid this problem the present invention provides a hollow tubular insert 3 which is fitted in the well 2 and provides an extended surface area for coating of the reagent. Such an insert may be made of plastics material such as polystyrene or polypropylene which is not constrained by requirements for optical clarity or mechanical strength. The insert may be made from a wide variety of materials some of which are optically opaque. Materials may be suitable for covalent coupling of reagents e.g. cellulose.

30 With reference now to the cross-section shown in Figure 2 the insert 3 is coated with a diagnostic reagent and placed in a well 2 of the microtitre plate 1. The insert is tubular with open ends and does not restrict or interfere with subsequent optical measurements taken by passing a beam of light 4 through the well 2 as used in the assay system.

Figures 3 to 9 illustrate various embodiments of well inserts.

Figure 3 illustrates in plan and side elevation an open ended tubular insert 3 extruded from a plastics material with ribs 5 extending vertically around the internal surface.

5           Figure 4 shows similar views to Figure 3 of a second embodiment of a well insert 3 which is extruded from plastics material and is formed with a zig-zag or pleated wall 6.

10           Figure 5 shows similar view to Figure 3 and 4 of a third embodiment of a tubular well insert 3 the inner wall being formed with raised surface bumps 7 arranged in vertical parallel lines.

15           Figure 6 shows a fourth embodiment of a well insert in plan and side elevation. The tubular insert 3 has a series of external spaced hoop projections 8 which provide a liquid-tight seal between the insert and well wall.

20           Figure 7 shows similar views of a fifth embodiment of a well insert 3 with external vertical ribs 9 spaced around the outer periphery of the tubular insert which provide access for the test sample to the space between the insert and the well wall.

25           Figure 8 is a side elevation of a sixth embodiment of a well insert 3 constructed from a helically formed plastics strip 10.

          Figure 9 is a similar view to Figure 8 of a seventh embodiment of a well insert formed as a tubular open rectangular mesh 11.

30           Embodiments of the well insert are illustrated in which the wall of the insert has an extended surface area which provide a means for enhanced coating of a reagent on its surface, prior to insertion in the well of a microtitre plate for the diagnostic test.

35           The inserts and microtitre plate may be suitably coloured to distinguish between different reagent batches.

          The well inserts can also be used with non-optical detection, such as radioactivity. In this case,

the well insert is removed after the assay and measured in a scintillation counter.

## CLAIMS:

1. A well insert for a microtitre plate comprising a hollow tubular member, the internal and/or external surface of which is shaped to provide an extended surface area for a reagent coated on the surface, and the surface chemistry of which allows coating or covalent coupling of reagents.
2. A well insert as claimed in Claim 1 wherein the insert is made from a plastics material.
3. A well insert as claimed in Claim 2 wherein the plastics material is polystyrene.
4. A well insert as claimed in Claim 2, wherein the plastics material is polypropylene.
5. A well insert as claimed in Claim 1, wherein the insert is made from cellulose.
6. A well insert as claimed in any of Claims 1 to 5, wherein the insert is formed with a series of internal vertical parallel ribs.
7. A well insert as claimed in any of Claims 1 to 5, wherein the insert is formed with a series of spaced external vertical ribs.
8. A well insert as claimed in any of Claims 1 to 5, wherein the insert is formed with a series of internal raised surface bumps.
9. A well insert as claimed in any of Claims 1 to 5, wherein the external surface is formed with a series of external spaced hoop projections arranged parallel to one another.
10. A well insert as claimed in any of Claims 1 to 5, wherein the hollow tubular member is formed by a helix.
11. A well insert as claimed in any of Claims 1 to 5, wherein the hollow tubular member is formed by an open rectangular mesh.
12. A microtitre plate comprising a plurality of wells incorporating one or more of the inserts claimed in any of the preceding Claims 5 to 11.
13. A well insert for a microtitre plate

substantially as hereinbefore described with reference to  
Figures 3 to 9 of the accompanying drawings.



1-2

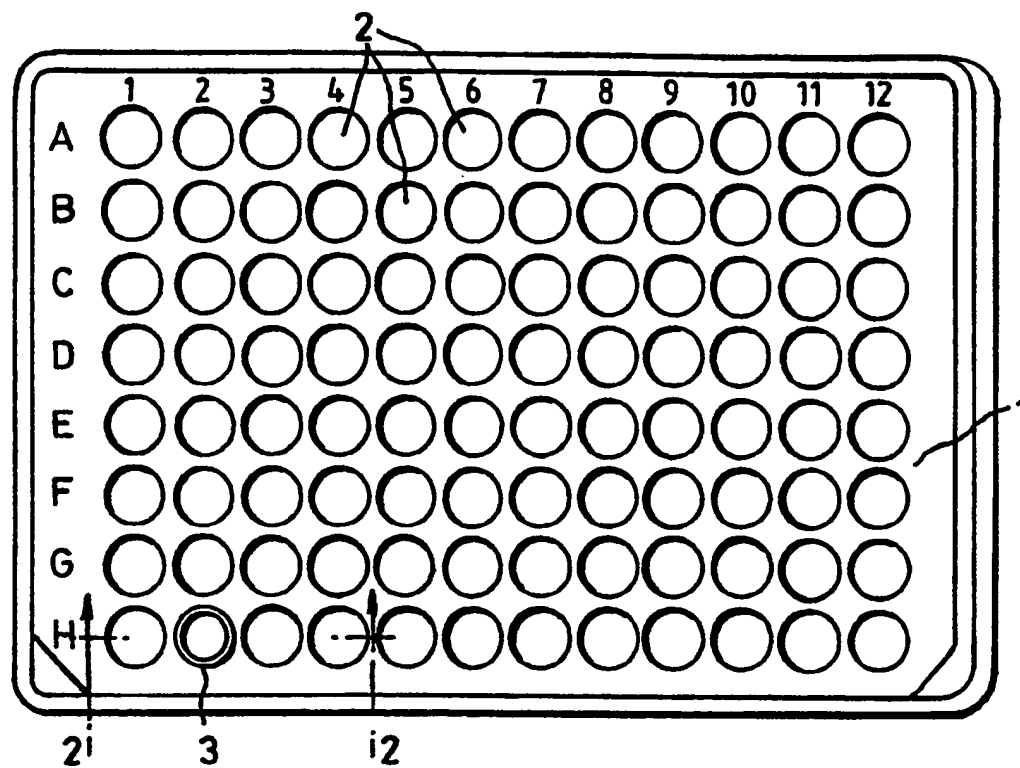


FIG.1.

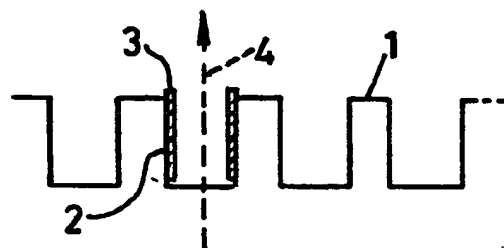
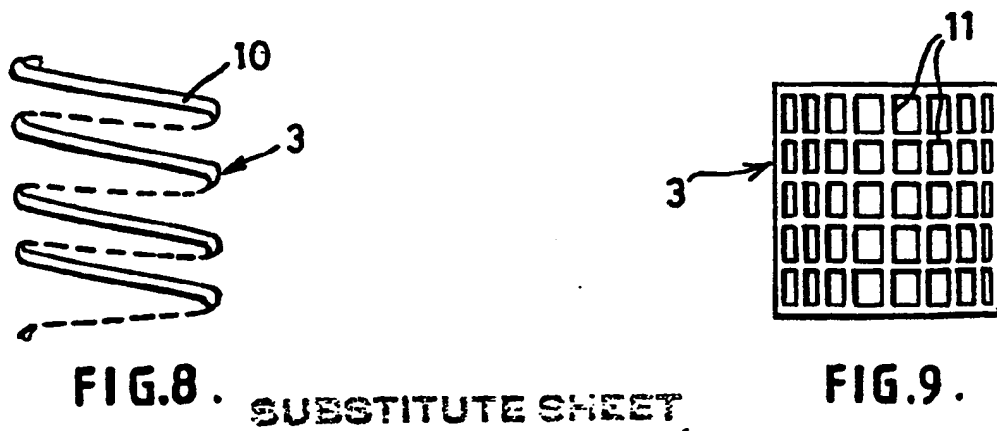
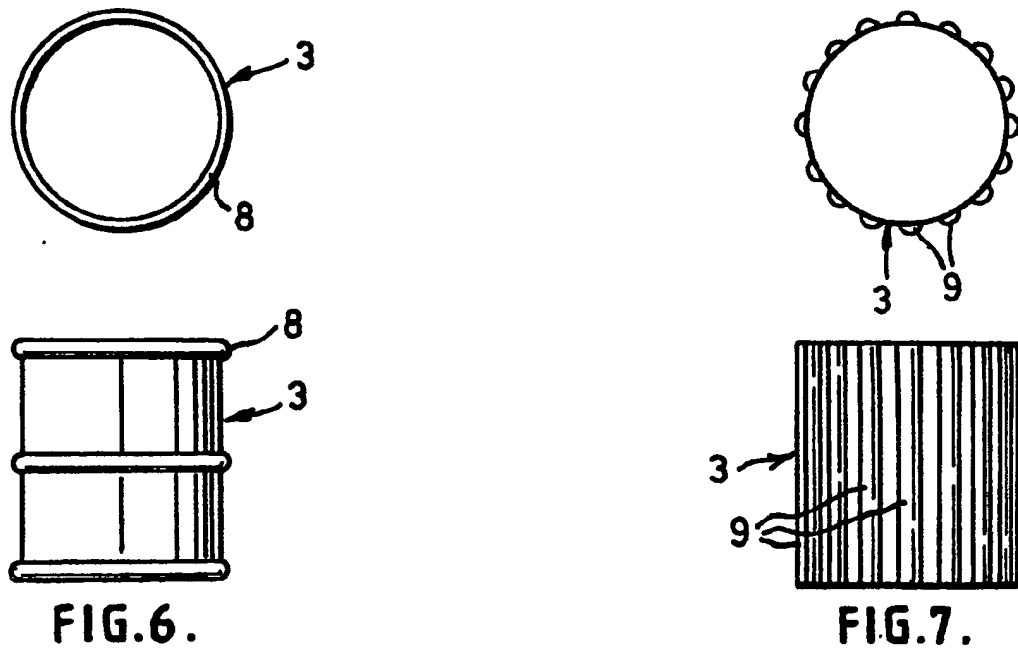
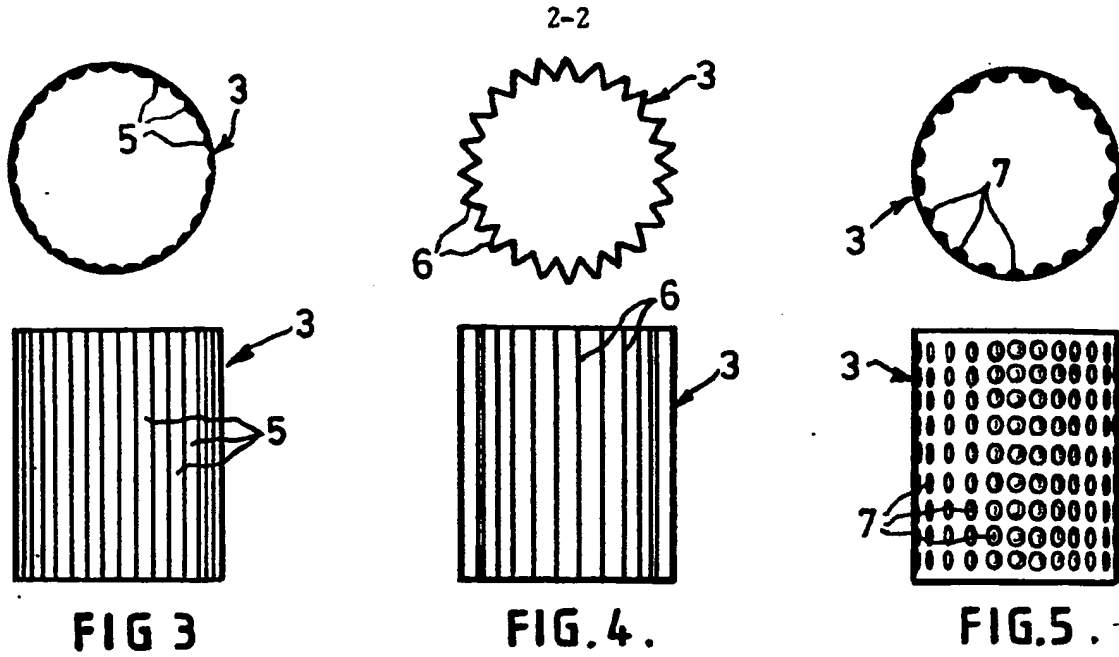


FIG.2.



SUBSTITUTE SHEET

# INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 90/01646

<b>I. CLASSIFICATION OF SUBJECT MATTER</b> (if several classification symbols apply, indicate all) <sup>6</sup> According to International Patent Classification (IPC) or to both National Classification and IPC IPC <sup>5</sup> : B 01 L 3/00, G 01 N 33/543																	
<b>II. FIELDS SEARCHED</b> <div style="text-align: center; border-top: 1px solid black; border-bottom: 1px solid black; margin: 5px 0;">Minimum Documentation Searched <sup>7</sup></div> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%; border-bottom: 1px solid black; padding: 5px;">Classification System</td> <td style="border-bottom: 1px solid black; padding: 5px;">Classification Symbols</td> </tr> <tr> <td style="padding: 5px;">IPC<sup>5</sup></td> <td style="padding: 5px;">G 01 N, B 01 L</td> </tr> </table> <div style="text-align: center; border-top: 1px solid black; border-bottom: 1px solid black; margin: 5px 0;">Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched <sup>8</sup></div>			Classification System	Classification Symbols	IPC <sup>5</sup>	G 01 N, B 01 L											
Classification System	Classification Symbols																
IPC <sup>5</sup>	G 01 N, B 01 L																
<b>III. DOCUMENTS CONSIDERED TO BE RELEVANT <sup>9</sup></b> <table style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 10%; border-bottom: 1px solid black; padding: 5px;">Category <sup>10</sup></th> <th style="width: 70%; border-bottom: 1px solid black; padding: 5px;">Citation of Document, <sup>11</sup> with Indication, where appropriate, of the relevant passages <sup>12</sup></th> <th style="width: 20%; border-bottom: 1px solid black; padding: 5px;">Relevant to Claim No. <sup>13</sup></th> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">X</td> <td style="padding: 5px;">           EP, A, 0296415 (PALL CORPORATION)            28 December 1988            see abstract; figure; column 4,            lines 48-52; column 6, lines 33-51;            column 10, lines 8-26  <div style="text-align: center;">--</div> </td> <td style="text-align: center; vertical-align: top; padding: 5px;">1,2,12</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">X</td> <td style="padding: 5px;">           FR, A, 2418457 (COMMISSARIAT A L'ENERGIE            ATOMIQUE)            21 September 1979            see page 3, line 12 - page 4, line 13;            figures 1,2  <div style="text-align: center;">--</div> </td> <td style="text-align: center; vertical-align: top; padding: 5px;">1,2,7,10</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">X</td> <td style="padding: 5px;">           FR, A, 2377629 (KOMMANDIITTIYHTIO            FINNPIPETTE OSMO A. SUOVANIEMI)            11 August 1978            see page 3, lines 21-32; page 4,            lines 3-6; page 5, lines 5-7, 19-21;            pages 13,15-19; figures 1-15  <div style="text-align: center;">--</div> </td> <td style="text-align: center; vertical-align: top; padding: 5px;">1,2,5,6-9, 12</td> </tr> <tr> <td colspan="2" style="text-align: right; padding: 5px;">./.</td> <td></td> </tr> </table>			Category <sup>10</sup>	Citation of Document, <sup>11</sup> with Indication, where appropriate, of the relevant passages <sup>12</sup>	Relevant to Claim No. <sup>13</sup>	X	EP, A, 0296415 (PALL CORPORATION) 28 December 1988 see abstract; figure; column 4, lines 48-52; column 6, lines 33-51; column 10, lines 8-26 <div style="text-align: center;">--</div>	1,2,12	X	FR, A, 2418457 (COMMISSARIAT A L'ENERGIE ATOMIQUE) 21 September 1979 see page 3, line 12 - page 4, line 13; figures 1,2 <div style="text-align: center;">--</div>	1,2,7,10	X	FR, A, 2377629 (KOMMANDIITTIYHTIO FINNPIPETTE OSMO A. SUOVANIEMI) 11 August 1978 see page 3, lines 21-32; page 4, lines 3-6; page 5, lines 5-7, 19-21; pages 13,15-19; figures 1-15 <div style="text-align: center;">--</div>	1,2,5,6-9, 12	./.		
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<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p><sup>14</sup> Special categories of cited documents: <sup>15</sup></p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"d" document member of the same patent family</p> </div> </div>																	
<b>IV. CERTIFICATION</b> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; border-bottom: 1px solid black; padding: 5px;">Date of the Actual Completion of the International Search</td> <td style="width: 50%; border-bottom: 1px solid black; padding: 5px;">Date of Mailing of this International Search Report</td> </tr> <tr> <td style="text-align: center; padding: 5px;">14th February 1991</td> <td style="text-align: center; padding: 5px;">01 MAR 1991</td> </tr> <tr> <td style="border-bottom: 1px solid black; padding: 5px;">International Searching Authority</td> <td style="border-bottom: 1px solid black; padding: 5px;">Signature of Authorized Officer</td> </tr> <tr> <td style="text-align: center; padding: 5px;">EUROPEAN PATENT OFFICE</td> <td style="padding: 5px;">Mme N. KUIPER </td> </tr> </table>			Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	14th February 1991	01 MAR 1991	International Searching Authority	Signature of Authorized Officer	EUROPEAN PATENT OFFICE	Mme N. KUIPER							
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III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, " with indication, where appropriate, of the relevant passages	Relevant to Claim No.
X	EP, A, 0197729 (D.P. KELLY) 15 October 1986 see page 3, lines 6-9; page 4, lines 7-29  --	1,2,4,12
A	US, A, 4795562 (J.W. WALSH) 3 June 1989 see figure 4, column 1, lines 14-25; column 6, lines 3-32  -----	11

**ANNEX TO THE INTERNATIONAL SEARCH REPORT  
ON INTERNATIONAL PATENT APPLICATION NO.**

GB 9001646

SA 41706

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 26/02/91  
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A- 0296415	28-12-88	US-A- 4828386 JP-A- 1152340	09-05-89 14-06-89
FR-A- 2418457	21-09-79	None	
FR-A- 2377629	11-08-78	BE-A- 862908 CH-A- 637219 DE-A, C 2801026 GB-A- 1571872 JP-A, B, C 53130422 SE-B- 444227 SE-A- 7800236 US-A- 4147752	13-07-78 15-07-83 20-07-78 23-07-80 14-11-78 24-03-86 15-07-78 03-04-79
EP-A- 0197729	15-10-86	None	
US-A- 4795562	03-01-89	None	